Remarks

Claims 519-559 are presently pending in the subject application.

Reconsideration and allowance are respectfully requested in view of the above amendments and the following remarks.

The specification has been amended herein to update the priority data.

Claims 480-518 are canceled herein without prejudice to the prosecution of the subject matter of these claims in this or a continuing application.

Claims 519-559 are newly added herein. Language directed to components useful for performing an amplification reaction has been moved to new, dependent claim 521 and replaced with language directed to a solid support for immobilizing a target nucleic acid present in a sample in new, independent claim 519. *See* specification at, for example, page 25, line 5 *et seq*. New claim 520 depends from claim 519 and recites that the solid support has a magnetic charge. *See* specification at, for example, page 26, lines 2-3. New claims 522-559 correspond to prior claims 481-518.

Rejection Under 35 U.S.C. § 103

Claims 480-518 stand rejected by the Examiner under 35 U.S.C. § 103 as being unpatentable over Carmo-Fonseca et al. (1991) EMBO 10(7):1863-1873, as evidenced by Iribarren et al. (1990) Proc. Natl. Acad. Sci. USA 87:7747-7751, in view of Tsang (U.S. Patent No. 5,837,442). Applicants respectfully traverse this rejection, to the extent that it may applied to any of new claims 519-559, for the following reasons.

This rejection rests on the Examiner's belief that Carmo-Fonseca discloses probe molecules having first and second base regions that hybridize to each other. The Examiner references Table 1 on page 1872 of Carmo-Fonseca but fails to provide evidence or reasoning that any of the oligonucleotides disclosed therein has complementary first and second base regions that form a hybrid. *See* MPEP § 2142 at 2100-28 (8th ed., Rev. 2, May 2004). Applicants previously questioned

whether the oligonucleotides of Table 1 of Carmo-Fonseca contain self-hybridizing regions in their Reply Under 37 C.F.R. § 1.114 dated October 16, 2006, thus shifting the burden to the Examiner to come forward with supporting evidence. Despite Applicants' request for such evidence, the Examiner's conclusion remains unsubstantiated.

To further distinguish the kit claims over the cited art, the new independent kit claim recites, in addition to the probe, a solid support for immobilizing the target nucleic acid sequence so that unbound nucleic acids and other components of the sample can be removed from the target nucleic acid sequence. This is important, since there would have been no motivation for combining the probes of Carmo-Fonseca with solid supports for immobilizing target nucleic acid sequences, since Carmo-Fonseca was directed to detecting snRNAs in live cells using an *in vivo* hybridization procedure. *See* Carmo-Fonseca at page 1865, col. 2. Additionally, since Carmo-Fonseca favored oligonucleotides made of 2'-O-allyl RNA because of their nuclease resistance and antisense properties, there is no motivation to use them in an *in vitro* hybridization procedure that includes means for removing sample components such as nucleases. *Id.* The same reasoning applies to the use of the claimed probe molecules in an amplification reaction.

The Examiner contends that claims 491 and 511 are unpatentable because Carmo-Fonseca teaches a probe having a conjugate molecule joined to the probe at a site located within the cluster of the first base region. To support this patentability determination, Table 1 of Carmo-Fonseca is cited by the Examiner. However, Carmo-Fonseca's description of the oligonucleotides in Table 1 states that these oligonucleotides were 5' end-labeled for the various experiments described. Thus, Applicants submit that Carmo-Fonseca does not teach a joining a conjugate to an internal location of an oligonucleotide.

The Examiner also urges that claims 496 and 516 are unpatentable because Carmo-Fonseca teaches a target nucleic acid comprising ribosomal RNA at page 1863, col. 2, in lines 4-8 of the final paragraph. The referenced section refers to snRNPs but not to ribosomal RNA.

Additionally, the Examiner concludes that claims 497 and 517 are unpatentable because Carmon-Fonseca teaches a target sequence having a double-stranded region. The Examiner does not identify a particular double-stranded target region which is targeted by one of the disclosed oligonucleotides, but merely states that snRNAs in general have hairpins regions which are double-stranded. This distinction is significant, however, because one of the advantages discovered by Applicants is the ability of 2'-O-alkyl modified probes to efficiently strand invade double-stranded regions of structured RNA molecules. *See* specification at page 8, lines 11-14.

Tsang does not teach, suggest or motivate the use of the claimed probe molecules in a kit or reaction mixture useful for conducting an *in vitro* reaction, such as an amplification reaction.

For the reasons set forth above, Applicants submit that the presently pending claims are fully patentable in view of the cited references, considered alone or in any combination.

Conclusion

In view of the amendments and remarks set forth herein, Applicants submit that the subject application is in condition for allowance and notice to that effect is respectfully requested.

Please charge any fees due in connection with this Reply, including the fee due for a three-month extension of time, to Deposit Account No. 07-0835 in the name of Gen-Probe Incorporated.

Respectfully submitted,

Date: June 27, 2007

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